(19) World Intellectual Property Organization

International Bureau





(43) International Publication Date 4 August 2005 (04.08.2005)

PCT

(10) International Publication Number WO 2005/070951 A1

(51) International Patent Classification⁷: C07J 1/00

(21) International Application Number:

PCT/US2005/001248

(22) International Filing Date: 14 January 2005 (14.01.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/536,944 16 January 2004 (16.01.2004) US

(71) Applicant (for all designated States except US): CEDAR-BURG PHARMACEUTICALS, INC. [US/US]; 870 Badger Circle, Grafton, WI 53024 (US).

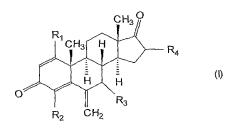
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): KUNNEN, Kevin

[US/US]; 4606 Queen Road, Plymouth, IN 46563-9718 (US). STEHLE, Nathan, W. [US/US]; 1335 16th Avenue, Apt. 9, Grafton, WI 53024 (US). WEIS, Scot, W. [US/US]; 4054 North 64th Street, Milwaukee, WI 53216 (US). PASCONE, John, M. [US/US]; 315 W. Thornapple Lane, Grafton, WI 53024 (US). PARIZA, Richard, J. [US/US]; 43323 N. Oakcrest Lane, Zion, IL 60099 (US). VAN ORNUM, Scott, G. [US/US]; 3244 Twin Creeks Road, Jackson, WI 53037 (US).

- (74) Agent: ROCHE, Richard, T.; Quarles & Brady LLP, 411 East Wisconsin Avenue, Milwaukee, WI 53202 (US).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,

[Continued on next page]

(54) Title: EXEMESTANE AND ITS INTERMEDIATES AND METHODS OF MAKING THE SAME



$$R_1$$
 CH_3 H H R_3 R_4 R_4 R_3 R_4

(57) Abstract: A method is provided for preparing an aromatase inhibitor of formula (I) wherein each of R_1 , R_2 , R_3 , R_4 , independently, is hydrogen, halogen or C_1 - C_6 alkyl. In one form, the aromatase inhibitor is exemestane wherein each of R_1 , R_2 , R_3 , R_4 is hydrogen. In the method, a compound of formula (II) wherein R_1 , R_2 , R_3 , R_4 are as defined above and R is alkylene, is reacted with a deprotonating agent and a compound of the formula R_5 SO₂X wherein R_5 is C_1 - C_5 alkyl and X is halogen so as to obtain a compound of formula (III) wherein R_1 , R_2 , R_3 , R_4 , R_5 are as defined above. The compound of Formula (III) is then reacted with a base to form an aromatase inhibitor of formula (I).



WO 2005/070951 A1



TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO,

SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.